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**REMARKS**

Reconsideration of this application in view of the following remarks is respectfully requested.

**I. Status of the claims**

Claims 1-5, 10-11, and 17 are pending in this case. Claims 6-9, 12-16, and 18-24 were canceled in response to the Office Action dated January 10, 2006.

**II. Rejections under 35 U.S.C. § 103 based on Sporeno in view of Newton**

Claims 1-5, 10-11, and 17 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Sporeno et al. (Cytokine, 6(3):255-264 (1994)) ("Sporeno") in view of Newton et al. (Mol. Biotech. 20:63-76 (2002)) ("Newton"). The Examiner alleged that Sporeno teaches a method for purifying a 6x histidine tagged cytokine with a four-helix bundle with a single step metal chelating column. The Examiner admitted that Sporeno does not teach the use of a heparin column before the metal chelating column. Nevertheless, the Examiner asserted that it would have been *prima facie* obvious to one of ordinary skill to modify Sporeno's metal chelating column method by applying Newton, which the Examiner alleged teaches a 2-step metal chelating column separation using a heparin column before the metal chelating column to eliminate contaminants. Applicants respectfully traverse this rejection.

Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness. "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP § 2142 (citing *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991)). The Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness on the basis of Sporeno in view Newton, principally because the Examiner has not established at least the first and second elements of the *prima facie* case.

Contrary to the Examiner's assertion, the claims are not obvious over Sporeno in view of Newton because one skilled in the art would not be motivated to combine Sporeno and Newton. Sporeno merely relates to purifying Onc M from urea solubilized bacterial cells using a Ni<sup>2+</sup> metal chelating column. See page 256, second column and page 262, first and second column. Contrary to the Examiner's position, there is no teaching, motivation or suggestion in Sporeno for removing contaminants before the metal chelating step, or that a heparin column is desirable for removing

contaminants. Indeed, Sporeno is completely silent with respect to a heparin column. Newton adds nothing that remedies the deficiencies in Sporeno's teachings. Newton merely relates to purification of a non-cytokine protein using heparin and metal chelating columns. Further, Sporeno itself does not provide any motivation to combine the teaching of Newton. One skilled in the art would not be motivated to combine a reference directed to purifying a non-cytokine (Newton) with a reference directed to purifying a cytokine (Sporeno) to arrive at the claims of the instant application directed to purifying cytokines. Thus, the claims cannot be obvious because Sporeno does not provide any motivation with a reasonable expectation of success to modify Sporeno with Newton.

It appears that the Examiner has simply used the Applicant's disclosure and claims as a blueprint. This is apparent since there is no motivation in the art to combine the references in the cited manner, and none is actually cited. For example, to motivate the combination of Sporeno and Newton, the Examiner stated that the majority of contaminating proteins are eliminated by adding the heparin column of Newton before a metal chelating column. Well, of course, contaminating protein are removed, as evidenced by Applicant's disclosure. But again, the art nowhere tells one of skill in the art to make that combination. The Examiner's statements regarding the asserted combination is simply an assertion that a method according to Applicant's claims and specification will perform as recited. There is no actual motivation in the art, and none is cited, to in fact make the asserted combination based on Sporeno and Newton.

This is the hindsight trap, wherein pieces of prior art are simply strapped together to match whatever is claimed. It is improper, it violates the law and the Federal Circuit has condemned this approach. Why is it improper? Because it is empty and can be used to cobble together any invention. The Examiner falls into exactly the same trap. Sporeno relates to purifying a cytokine using only a metal chelating column cell but provides no teaching or suggestion that an additional contaminant removal step using a heparin column is desirable or even necessary. Thus, Sporeno fails to teach purifying a cytokine using a heparin column and a metal chelating column. So the Examiner finds a reference that does teach such a heparin column and simply states that if we combine this with Sporeno, voilà, Sporeno's method is now the claimed method.

A §103 rejection based on a combination of references requires a **motivation in the art**, not just a restatement of the beneficial result that was foretold by the Applicant's disclosure and claims. Regarding the Examiner's hindsight approach, the Court of Appeals for the Federal Circuit has said the following:

A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. Close adherence to this methodology is especially important in cases where the very ease with

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which the invention can be understood may prompt one "to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher."

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Most if not all inventions arise from a combination of old elements. Thus, every element of a claimed invention may often be found in the prior art. However, **identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention.** Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant.

*In re Kotzab*, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000) (citations omitted).

Thus, it is respectfully submitted that although the Examiner notes that combining elements to yield the invention would be beneficial, the Examiner does not actually cite any motivation in the art to make that combination, for there exist none indeed. Thus, Applicants respectfully request favorable reconsideration of claims 1-5, 10-11, and 17.

Accordingly, withdrawal of the § 103 rejection of the claims based on Sporeno in view of Newton is in order and is respectfully requested.

### III. Conclusion

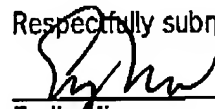
In light of the above discussion, the Applicants submit that the claims are in allowable condition. A Notice to this effect is respectfully requested.

Reconsideration of this application is respectfully requested and a favorable determination is earnestly solicited. The Examiner is invited to contact the undersigned representative if the Examiner believes this would be helpful in expediting the allowance of this application.

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